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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/939,518	08/24/2001	Mark J. Jaroszeski	93004	2429

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EXAMINER

ANGELL, JON E

ART UNIT PAPER NUMBER

1635

DATE MAILED: 06/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/939,518

Applicant(s)

JAROSZESKI ET AL.

Examiner

Jon Eric Angell

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,4,6,8,10 and 21-28 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,4,6,8,10 and 21-28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____.  |

### **DETAILED ACTION**

Claims 1, 2, 4, 6, 8, 10 and 21-28 are currently pending in the application.

Applicant is advised that the Notice of Allowance mailed is vacated. If the issue fee has already been paid, applicant may request a refund or request that the fee be credited to a deposit account. However, applicant may wait until the application is either found allowable or held abandoned. If allowed, upon receipt of a new Notice of Allowance, applicant may request that the previously submitted issue fee be applied. If abandoned, applicant may request refund or credit to a specified Deposit Account.

Prosecution on the merits of this application is reopened on claims 1, 2, 4, 6, 8, 10 and 21-28, which are considered unpatentable for the reasons indicated below.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4, 6, 8, 10 and 21-28 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 21 recite the phrase, "low level electric field". The specification does not explicitly define "low level electric field". The specification does indicate "High field strengths,

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100V/cm and greater, were used exclusively in the past” (see page 3, line 6), indicating that field strengths of 100V/cm or greater are not low-level field strengths.

It is respectfully pointed out that claims 1 and 21 are not limited to any particular field strength other than low-level field strength. Claims 4 and 23, which depend from claims 1 and 21, respectively, explicitly indicate that the low level electric field has a field strength comprising 200V/cm or less. Therefore, the field strength of a “low level electric field” must be at least 200V/cm. Considering the specification indicates that 100V/cm is a “high field strength” it is unclear how a “low level field strength” could be anything higher than 100V/cm (such as 200V/cm). Therefore, the claims are indefinite.

It is noted that amending claims 1 and 21 to delete the phrase “low level electric field” and to include a specific field strength (such as 200V/vm or less) would obviate this rejection.

In the absence of an explicit definition in the specification, the phrase “low level electric field” is interpreted to encompass any field strength that an artisan skilled in the field would consider “low level”. As indicated below, Nolan (an artisan skilled in the field) considers about 300V/cm to about 600V/cm to be a “low level electric field” (e.g., see claim 1 of US 6,800,484).

Therefore, the limitation “low level electric field” will be interpreted as any electric field that is about 600V/cm or less.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 6, 10 rejected under 35 U.S.C. 102(e) as being anticipated by US 6,800,484 B2 (Nolan et al.).

The instant claims are drawn to a method for facilitating the delivery of a molecule into a target tissue consisting essentially of the steps of: introducing into a target tissue comprising a cell; applying an electric field to the target tissue, the application of the electric field consisting of a single low level electric field applied for a duration of 10ms to 20 minutes; and, effecting a change in porosity of the cell of the target tissue in response to the application of the electric field, the change in porosity sufficient to facilitate entry of a desired molecule into an interior of the cell (claim 1); wherein the duration of the applying step is in a range of 100ms to 100sec (claim 2); wherein the electric field can be, among others, a square pulse or exponential pulse (claim 6); and wherein the target tissue can be, among others, skin, tumor or brain tissue (claim 10).

Nolan teaches a method for introducing a nucleic acid or polypeptide into a cell by contacting the cell with the nucleic acid or polypeptide and applying a low electrical field impulse for a long pulse length (e.g., see abstract). Nolan specifically teaches A method for introducing a nucleic acid into a cell of a mammalian subject, comprising: contacting the cell an

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isolated nucleic acid sequence and applying to the cell a low electrical field impulse of about 300 V/cm to about 600 V/cm for a long pulse length of about 10ms to about 100ms, wherein the impulse is of sufficient duration and strength to allow introduction of the nucleic acid into the cell (e.g., see claim 1); wherein the electrical impulse is a square wave pulse or an exponential wave pulse (e.g., see claim 9); and wherein the electrical impulse is a single (i.e., one) electrical pulse (e.g., see claim 11) (also see column 11, lines 52-67; and column 12, lines 1-30), and teaches a working example wherein a nucleic acid is delivered into a cell using a single low field strength pulse (e.g., see column 13, lines 17-25). Nolan also teaches that the target cell can be, among others, tumor cells or skin cells (e.g., see column 3, lines 4-9) and also teaches that the nucleic acid can be delivered to mammalian cells in vivo by injection of the nucleic acid sequence, preferably at or near the site of electroporation (e.g., see column 3, lines 53-61).

Therefore, Nolan anticipates the instant claims.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

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evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,800,484 B2 (Nolan et al.) in view of Mir et al. (PNAS Vol. 96:4262-4267; April 1999; previously cited).

The instant claims are drawn to a method for facilitating the delivery of a molecule into a target tissue consisting essentially of the steps of: introducing into a target tissue comprising a cell; applying an electric field to the target tissue, the application of the electric field consisting of a single low level electric field applied for a duration of 10ms to 20 minutes; and, effecting a change in porosity of the cell of the target tissue in response to the application of the electric field, the change in porosity sufficient to facilitate entry of a desired molecule into an interior of the cell (claim 1); wherein the introducing step comprises the step can be, among others, syringe injection (claim 8).

As indicated above, Nolan teaches a method for introducing a nucleic acid or polypeptide into a cell by contacting the cell with the nucleic acid or polypeptide and applying a low electrical field impulse for a long pulse length (e.g., see abstract). Nolan specifically teaches A method for introducing a nucleic acid into a cell of a mammalian subject, comprising: contacting the cell an isolated nucleic acid sequence and applying to the cell a low electrical field impulse of about 300 V/cm to about 600 V/cm for a long pulse length of about 10ms to about 100ms,

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wherein the impulse is of sufficient duration and strength to allow introduction of the nucleic acid into the cell (e.g., see claim 1); and wherein the electrical impulse is a single (i.e., one) electrical pulse (e.g., see claim 11) (also see column 11, lines 52-67; and column 12, lines 1-30), Nolan also teaches that the nucleic acid can be delivered to mammalian cells in vivo by injection of the nucleic acid sequence, preferably at or near the site of electroporation (e.g., see column 3, lines 53-61).

Nolan does not explicitly teach that the nucleic acid is delivered by syringe injection.

Mir teaches a method for facilitating a delivery of a desired molecule, here a nucleic acid plasmid, into a target tissue comprising a cell by administering the desired molecule to a subject and applying an electric field to the target cell (e.g., see abstract; and Fig 1, page 4264).

Mir specifically teaches that the desired molecule (here a nucleic acid) is delivered to the target tissue by syringe injection (see p. 4263, first column under “DNA Injection and Electric-Pulse Delivery”).

Since the only limitation missing from Nolan is the express teaching that the desired molecule (e.g., a nucleic acid) is delivered by syringe injection, and considering that Mir teaches that syringe injection may be used to deliver a nucleic acid to a site for electroporation delivery, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Nolan and Mir to create the claimed invention with a reasonable expectation of success.

The motivation to combine the references to create claimed invention is provided by Mir who teaches that syringe injection is one specific means of delivering a nucleic acid to a target site for electroporation delivery into a cell.



***Conclusion***

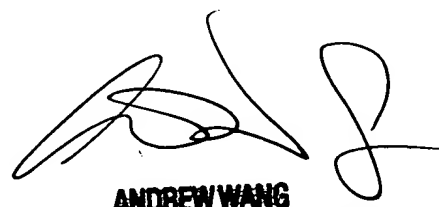
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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